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Levels of Cadmium and Lead in Blood in Relation to Smoking, Sex, Occupation, and Other Factors in an Adult Population of the FRG*

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Summary. Levels of cadmium (CdB) and lead (PbB) were determined in the blood of 579 60-65 year-old residents of Cologne and two small cities near Cologne. CdB-levels in cigarette smokers are on the average 3-4 times higher than in non-smokers (geometric means: non-smokers, 0.44 µg/l; ≤10 cigarettes/d, 1.16 µg/l; >10 cigarettes/d, 1.85 µg/l). The results indicate that, with regard to the internal dose, cadmium exposure via smoking may contribute even more than does exposure via food. PbB-levels (geometric mean: 8.49 µg/100 ml; range: 2.9-30.3 µg/100 ml) are in the acceptable range as defined by the CEC reference values. Male smokers have on the average slightly higher PbB-levels than male non-smokers. In women PbB-levels are on the average lower than in men.

Key words: Cadmium in blood - Lead in blood - Smoking - Sex - Occupation

Introduction

It has been recognized in the last few years that smoking is an important source of exposure to cadmium for smokers. Tobacco contains relatively high cadmium concentrations, varying between 1 and 2 µg per cigarette in cigarette brands usually smoked in the West-European countries [1]. 0.1-0.2 µg cadmium are inhaled by smoking one cigarette (1). Smokers have on the average higher levels of cadmium in blood (2-9), urine [8, 10], kidney [8, 11-15], and liver [8, 11, 15]. Placental cadmium levels are higher in smoking than in non-smoking women (16). It has been concluded that cadmium exposure via smoking may contribute as much as does exposure via food with regard to the internal dose [17].

Smoking has also been shown to represent a source of exposure to lead. However, in contrast to cadmium, smoking makes only a small contribution to

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the total intake of lead [18]. Several researchers have reported higher blood-lead (PbB) levels for smokers than for non-smokers [3, 5, 19-21], while others were unable to confirm such an association [22-24]. Thus, a WHO expert group recently concluded that the influence of smoking on PbB-levels has not been fully evaluated [18].

In 1982 we had the opportunity to evaluate data on PbB- and CdB-levels of an adult population ($n=579$ subjects), who participated in a health surveillance programme performed to investigate the effect of urban air pollution on human health [25]. These data allowed us to study the effect of smoking and various other factors (sex, place of residence, occupation, passive smoking) on PbB- and CdB-levels in adult males and females. Multiple regression analysis was used to assess the effect of various variables on the variation of PbB and CdB.

Subjects and Methods

Subjects

Two hundred and eighty-five 60-65 year-old residents (146 men and 139 women) from Cologne and two hundred and ninety-four 60-65 year-old residents (140 men and 154 women) of two small cities near Cologne (Meckenheim, about 15 000 inhabitants; Rheinbach, about 22 000 inhabitants) participated in the study. The subjects were randomly selected from the municipal registries of inhabitants. Each participant was asked to complete a questionnaire in order to obtain information on smoking, passive smoking at home or at the work place, occupation, place of residence and the subject's health status. The questionnaires were checked afterwards by a physician.

Methods

Blood samples were taken by venipuncture using disposable syringes ("Monovetten", Sarstedt, Nümbrecht, FRG) and needles, which were checked previously to be free of heavy metal contamination. EDTA was used as an anticoagulant. The syringes were equipped with uncoloured caps, since red caps, which are normally used in commercially available EDTA-containing syringes, contain small amounts of cadmium, which could lead to a contamination of the samples. Blood samples were transferred to the laboratory the same day, kept overnight at 4°C, and deep-frozen in liquid nitrogen the following day within the syringes. Samples were stored at -20°C and thawed prior to analysis. Coagulation is prevented by this procedure.

PbB- and CdB-levels were measured by electrothermal atomic absorption spectrophotometry (Perkin Elmer Model 5000, equipped with a HGA 500 graphite furnace and an automatic sampling system AS 1) according to the method of Stoeppler et al. [26]. Calibration was performed with the aid of a calibration curve based on human blood. Results are given in $\mu\text{g/l}$ for CdB and $\mu\text{g}/100\text{ ml}$ for PbB.

All analyses were carried out under strict quality control conditions. Internal quality control was performed by the use of two blood samples with different levels of lead and cadmium, which were deep-frozen and examined with each analytical series. Data on the evaluation of the within run and between-run precision of CdB and PbB determinations are reported in Table 1. The detection limit for CdB was 0.18 $\mu\text{g/l}$.

External quality control was performed by the use of control blood for metals, concentration 1 (Behring, Marburg, FRG; Lot No. 62 0301). Means from 20 determinations on 5 different days were $5.30 \pm 0.45\text{ }\mu\text{g/l}$ for CdB and $41.5 \pm 2.75\text{ }\mu\text{g}/100\text{ ml}$ for PbB. The values given on the certificate of analysis were 5.5 $\mu\text{g/l}$ for CdB (confidence range: 4.8-6.2 $\mu\text{g/l}$) and 40.8 $\mu\text{g/l}$ for PbB (confidence range 39.5-42.0 $\mu\text{g/l}$).

External quality control was further performed by participation in the interlaboratory quality control programme on blood-lead analysis organized by the Health and Safety

Table 1. Within-run and between-run precision of CdB- and PbB-analysis

		<i>n</i>	\bar{x}	SD	rel. SD (%)
CdB ($\mu\text{g/l}$)	Within run	16	2.28	0.10	4.6
	Between-run	19	0.42 ^a	0.09	20.7
		19	2.41 ^b	0.13	5.5
		5	5.09 ^d	0.47	9.3
PbB ($\mu\text{g}/100\text{ ml}$)	Within-run	16	9.53	0.39	4.0
	Between-run	19	14.28 ^a	0.80	5.6
		19	29.47 ^c	1.33	4.5
		5	41.22 ^d	3.08	7.5

^a Human blood

^b Human blood spiked with 2 μg Cd/l

^c Human blood spiked with 15 μg Pb/100 ml

^d Control blood 1 for metals (Behring)

Table 2. CdB- and PbB-levels in 60-65 year-old residents ($n=579$) of Cologne, Meckenheim, and Rheinbach, FRG

	Arithmetic mean	SD	Geometric mean	Median	Range
CdB ($\mu\text{g/l}$)	0.85	0.90	0.61	0.53	<0.2- 6.5
PbB ($\mu\text{g}/100\text{ ml}$)	9.00	3.30	8.49	8.39	2.9-30.3

Directorate of the Commission of the European Communities in 1981. Our results on PbB and CdB determinations were reasonably consistent with the medians of the results of the other participating laboratories throughout this programme.

Each blood sample was measured in duplicate on two different days. The agreement between the first (x) and second (y) determination was as follows: PbB: $\log y = 1.0039 \log x - 0.0138$; $r = 0.97$; $n = 579$; rel. SD = 6.5% (PbB 2.9-30.3 $\mu\text{g}/100\text{ ml}$); CdB: $\log y = 0.9863 \log x - 0.0039$; $r = 0.96$; $n = 579$; rel. SD = 18% (CdB $\leq 0.5\text{ }\mu\text{g/l}$) and 10% (CdB $> 0.5\text{ }\mu\text{g/l}$). Means of the first and the second determination were used for statistical analyses.

Statistical Methods

Stepwise multiple regression analysis [27] was carried out using the logarithms of PbB- and CdB-levels to evaluate which independent variables could best explain the variation of the dependent variables (log PbB and log CdB).

Results

The means, medians and ranges of CdB- and PbB-levels are presented in Table 2.

Using stepwise multiple regression analysis, the effect of the following independent variables on CdB- and PbB-levels was studied: smoking, occupation, place of residence, and sex. The subjects were subdivided at least into three groups:

Table 3. Stepwise multiple regression analysis of the effect of various variables on CdB-levels in 60-65 year-old males and females ($n=546^a$)

Source of variation	df	SQ	F	% of the total variation explained	Level of significance
Cigarette smoking	1	30.466	653.75	54.58	$P<0.001$
Occupation	1	0.004	0.09	0.01	NS
Place of residence	1	0.003	0.07	0.01	NS
Sex	1	0.035	0.74	0.06	NS
Not explained	541	25.310			

^a Cigarette, cigar, and/or pipe smokers ($n=27$) and subjects with incomplete records ($n=3$) were not considered in this evaluation. Three outliers had to be eliminated for statistical reasons

Table 4. Stepwise multiple regression analysis of the effect of various variables on PbB-levels in 60-65 year-old males and females ($n=544^a$)

Source of variation	df	SQ	F	% of the total variation explained	Level of significance
Cigarette smoking	1	0.496	26.29	4.63	$P<0.001$
Occupation	1	0.024	1.24	0.22	NS
Place of residence	1	0.001	0.07	0.01	NS
Sex	1	0.955	55.61	8.90	$P<0.001$
Interaction smoking* Sex	1	0.099	5.84	0.93	$P<0.001$
Not explained	538	9.154			

^a See footnote to Table 3. Five outliers had to be eliminated for statistical reasons

(1) non-smokers ($n=415$), (2) light smokers (1-10 cigarettes/d; $n=53$); (3) heavy smokers (>10 cigarettes/d; $n=81$). "Mixed smokers" (Cigarette, cigar, and/or pipe smokers; $n=27$) were omitted and not considered in this evaluation. As regards occupation, the subjects were subdivided into two groups: (1) manual workers who might be occupationally exposed to heavy metals; (2) clerks, office-workers, pensioners, housewives etc. without potential occupational exposure to heavy metals. Concerning the place of residence, the subjects were subdivided into two categories: residents of urban and rural areas.

Results of the stepwise multiple regression analysis are shown in Tables 3 and 4. About 55% of the variation of CdB-levels is explained by cigarette smoking. The other variables are not significant predictors of CdB-levels.

Geometric mean values of CdB-levels in relation to smoking habits, occupation, and sex are shown in Table 5. Light and heavy smokers have on the average nearly 3 and 4 times, respectively, more cadmium in blood than non-smokers. The 95th percentile of the CdB-levels of non-smokers was calculated to be $0.98 \mu\text{g/l}$. The frequency distribution of CdB-levels in smokers and non-smokers

Table 5. Geometric means of CdB-levels ($\mu\text{g/l}$) in relation to cigarette smoking, occupation and sex

Smoking habits	Clerks, officeworkers, pensioners, housewives etc.				Manual workers				Total	
	Males		Females		Males		Females		Total	
	n	\bar{x}	n	\bar{x}	n	\bar{x}	n	\bar{x}	n	\bar{x}
Non-smokers	165	0.44	234	0.44	13	0.53	2	0.38	41	0.44
1-10 cig/d	18	0.99	32	1.32	2	0.61			52	1.16
>10 cig/d	56	1.88	22	1.82	2	1.68			80	1.85

Table 6. Geometric means of PbB-levels ($\mu\text{g/100 ml}$) in relation to cigarette smoking, occupation, and sex

Smoking habits	Clerks, officeworkers, pensioners, housewives etc.				Manual workers				Total	
	Males		Females		Males		Females		Total	
	n	\bar{x}	n	\bar{x}	n	\bar{x}	n	\bar{x}	n	\bar{x}
Non-smokers	166	9.20	232	7.35	13	9.59	2	5.25	179	9.23
1-10 cig/d	18	9.98	31	8.53	2	10.12			20	10.00
>10 cig/d	57	9.92	21	9.36	2	9.54			59	9.90
									21	9.36

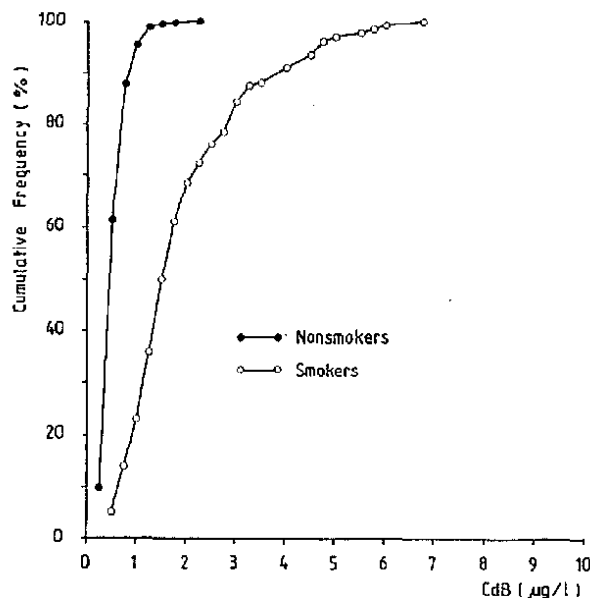


Fig. 1. Frequency distribution of CdB-levels in non-smokers and smokers

Compared to CdB, the effect of smoking on PbB-levels is much smaller. Male smokers have on the average slightly higher PbB-levels than non-smokers (Table 6). However, in females the increase due to smoking is more pronounced than in males. Smoking, sex, and the interaction of smoking and sex are significant predictors of PbB-levels that account for about 15% of the total variation of PbB-levels (Table 4). Women have on the average lower PbB-levels than men.

The effect of passive smoking on CdB- and PbB-levels was studied in 414 non-smokers. CdB- and PbB-values of subjects, who were exposed to cigarette smoke at home or at the work place, did not differ significantly from those of 'non passive-smokers'.

There is a weak, but statistically significant, linear correlation between PbB and CdB. The correlation coefficient was calculated to be 0.30 ($P < 0.001$; $n = 576$).

Discussion

CdB- and PbB-levels are in the same range as observed in numerous other studies [2-5, 7, 9, 19-21, 29] and indicate an overall exposure to lead and cadmium as may be expected in West-European communities with no habit of daily wine drinking or elevated environmental levels of lead and cadmium due to industrial emissions. The distribution of PbB-levels is fully within the acceptable range as defined by the reference values of the CEC-Directive on the biological screening of the population for lead [28]. Compared to a previous study, which we carried out in the same area [19], PbB-levels found in this study are slightly lower. This difference presumably is a systematic one since different analytical techniques were used in the two studies.

The present investigation confirms the results of other studies that smokers have higher levels of cadmium and lead in blood than non-smokers [2-9, 19-21]. Whereas PbB-levels are only slightly increased in smokers (by about 10% in males and 30% in females), the increase of CdB is much more pronounced. CdB-levels in smokers are on the average 3 to 4 times higher than in non-smokers. This difference is of the same order of magnitude as has been reported in some previous studies [2, 4, 7]. Other investigators have found smaller differences between smokers and non-smokers [3, 5, 6, 8, 9]. Since CdB-levels reflect current exposure to cadmium, our results suggest that cadmium exposure via smoking may contribute even more to the absorbed dose than does exposure via food.

The results of this study confirm our previous observation (19) that manual workers have on the average slightly higher PbB-levels than clerks, office-workers, and other "white-collar" workers. Since PbB and CdB reflect current exposure to these metals, this may be due to a slightly higher degree of exposure of these subjects at home or at the workplace. However, due to the small number of manual workers in our study population, this effect does not reach a level of statistical significance in the multiple regression analysis. CdB-levels in male non-smokers were also slightly higher in manual workers as compared to non-smoking male clerks, pensioners etc. (Table 5).

This study also confirms previous observations that men have on the average higher PbB-levels than women [30, 31]. It has been suggested that this difference is, at least in part, attributable to the higher haematocrit values and the higher food consumption of men [18]. An interesting observation is that the increase of PbB-levels due to smoking is more pronounced in women than in men. Thus, the interaction of smoking and sex makes a highly significant contribution to the total variation of PbB-levels (Table 4). Another interesting observation is that PbB-levels of the urban and "rural" population do not differ significantly in this study.

Unfortunately no data on the alcohol consumption of the subjects were available to us to test the hypothesis suggested by Grandjean et al. [20] that the increase of PbB-levels in smokers can, for the most part, be explained by an augmented alcohol intake in smokers. Alcoholic beverages, particularly wine, may contain significant amounts of lead. Thus, if smokers consume more alcoholic beverages than non-smokers, alcohol consumption could be a confounding factor in the relationship between smoking and PbB-levels.

Our results on cadmium exposure via cigarette smoking obtain additional significance when regarded with respect to recent results on the carcinogenicity of cadmium aerosols in Wistar rats [32]. Based on these results it has been suggested that cadmium in cigarette smoke may be a factor in the causation of lung cancer in cigarette smokers.

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